



Complete Summary

GUIDELINE TITLE

(1) 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. (2) 2009 addendum.

BIBLIOGRAPHIC SOURCE(S)

2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. 2009 addendum. Hagerstown (MD): American Society for Colposcopy and Cervical Pathology; 2009. 3 p. [5 references]

Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D, 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. Am J Obstet Gynecol 2007 Oct;197(4):346-55. [81 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wright TC Jr, Cox JT, Massad LS, Twiggs LB, Wilkinson EJ. 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. JAMA 2002 Apr 24;287(16):2120-9.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Atypical squamous cells
 - Of undetermined significance (ASC-US)
 - Cannot exclude high-grade squamous intraepithelial lesion (HSIL) (ASC-H)
- Low-grade squamous intraepithelial lesion (LSIL)
- HSIL
- Atypical glandular cells (AGC)

GUIDELINE CATEGORY

Management
Prevention
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Pathology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Plans
Managed Care Organizations
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To provide evidence-based consensus guidelines for the management of women with abnormal cervical cancer screening tests
- To update the 2001 consensus guidelines for the management of women with cervical cytological abnormalities

TARGET POPULATION

Women with abnormal cervical cancer screening tests

INTERVENTIONS AND PRACTICES CONSIDERED

Management of Atypical Squamous Cells of Undetermined Significance (ASC-US)

1. Repeat cervical cytology testing
2. Colposcopy

3. Human papillomavirus deoxyribonucleic acid (HPV DNA) testing

Management of Atypical Squamous Cells, Cannot Exclude High-Grade Squamous Intraepithelial Lesion (HSIL) (ASC-H)

1. Colposcopy
2. HPV DNA testing
3. Repeat cervical cytology testing

Management of Low-Grade Squamous Intraepithelial Lesion (LSIL)

1. Colposcopy
2. Endocervical sampling, if indicated
3. Repeat cervical cytological testing
4. HPV DNA testing

Management of High-Grade Squamous Intraepithelial Lesion (HSIL)

1. Loop electrosurgical excision or colposcopy
2. Review of colposcopy and cytology results
3. Diagnostic excisional procedure
4. Biopsy

Management of Atypical Glandular Cells

1. Colposcopy with endocervical sampling
2. Endometrial sampling
3. HPV DNA testing, if indicated
4. Repeat cytologic testing combined with HPV DNA testing, if indicated

Note: See the "Major Recommendations" field for the interventions specific to a special population, such as adolescent, immunosuppressed, postmenopausal, or pregnant women.

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of testing (colposcopy, human papillomavirus (HPV), cervical cytology, endocervical sampling, endometrial sampling)
- Rate of invasive cervical cancer after treatment
- Rate of recurrent/persistent atypical squamous cells
- Rate of recurrent/persistent squamous intraepithelial lesions
- Rate of recurrent/persistent atypical glandular cells (AGC)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original 2001 Guideline

The guideline developer performed searches of the U.S. Library of Medicine's MEDLINE database for English-language articles published between 1988 and 2001. Abstracts of articles were reviewed to determine their relevance; relevant articles were reviewed to determine whether they fulfilled a minimum, pre-determined scientific standard. In instances in which published data pertaining to a key issue were missing, scant, or conflicting, expert opinions expressed on an open Internet bulletin board or by members of the working group were used to help formulate the guidelines.

In addition to electronic searches, experts (committee members) were queried to identify studies not listed in MEDLINE, such as those in the *Journal of Lower Genital Tract Disease*. Also, important to note that conference participants also introduced data and expert opinion. This was especially the case for then-unpublished NCI Atypical Squamous Cells of Undetermined Significance/Low-grade Squamous Intraepithelial Lesion Triage Study (ALTS) data.

2006 Update

The process used to develop the 2006 Consensus Guidelines was similar to that for the previous guidelines. Working groups reviewed literature published after 2000.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence*

- I. Evidence from at least one randomized controlled trial.
- II. Evidence from at least one clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), or from multiple time-series studies, or dramatic results from uncontrolled experiments.
- III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

*Modified from Gross PA, Barrett TL, Dellinger EP, et al. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Dis 1994;18:421 and Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001;32:8511.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

From September 18 through 19, 2006, the American Society for Colposcopy and Cervical Pathology (ASCCP) hosted a consensus conference in Bethesda, MD, to develop revised evidence-based consensus guidelines for managing women with abnormal cervical cancer screening tests. To ensure that the guidelines reflect the needs of the diverse array of clinicians providing cervical cancer screening, the consensus conference included expert representatives from 29 organizations and professional societies. Input from the professional community at large was obtained by using an Internet-based bulletin board.

At the consensus conference, guidelines with supporting evidence were presented and underwent discussion, revision, and approval.

Although the guidelines are based on evidence whenever possible, for certain clinical situations, there is limited high quality evidence, and in these situations the guidelines have, by necessity, been based on consensus expert opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation*

- A. Good evidence for efficacy and substantial clinical benefit support recommendations for use.
- B. Moderate evidence for efficacy or only limited clinical benefit supports recommendation for use.
- C. Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds.
- D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.
- E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

Terminology**

Recommended: Good data to support use when only one option is available.

Preferred: Option is the best (or one of the best) when there are multiple other options.

Acceptable: One of multiple options when there are either data indicating that another approach is superior or when there are no data to favor any single option.

Unacceptable: Good data against use.

*Modified from Gross PA, Barrett TL, Dellinger EP, et al. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Dis 1994;18:421 and Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001;32:8511.

**The assignment of these terms represents an opinion ratified by vote by the Consensus Conference.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines were posted on the American Society for Colposcopy and Cervical Pathology (ASCCP) Internet Web site bulletin boards for public comment. At the consensus conference, guidelines with supporting evidence were presented and underwent discussion, revision, and approval.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The ratings of the strength of recommendation (A-E), the quality of the evidence (I-III), and terminology used by the consensus conference (recommended, preferred, acceptable, unacceptable) are repeated at the end of the "Major Recommendations" field.

Note from American Society for Colposcopy and Cervical Pathology (ASCCP): Recommendations for managing atypical squamous cells of undetermined significance and low-grade squamous intraepithelial lesion (LSIL) are essentially unchanged since 2001. Changes were made for managing these conditions in adolescents for whom cytological follow-up for 2 years was approved. Recommendations for managing high-grade squamous intraepithelial lesion (HSIL) and atypical glandular cells (AGC) also underwent only minor modifications. More emphasis is placed on immediate screen-and-treat approaches for HSIL. Human papillomavirus (HPV) testing is incorporated into the management of AGC after their initial evaluation with colposcopy and endometrial sampling. The 2004 Interim Guidance for HPV testing as an adjunct to cervical

cytology for screening in women 30 years of age and older was formally adopted with only very minor modifications.

2009 Addendum: Based on the data available at the time, the 2006 Consensus Guidelines included a recommendation that in cytology negative women 30 years and older who are HPV deoxyribonucleic acid (DNA) positive (for any of the 13 or 14 high-risk types of HPV detected by the high-risk HPV assays) molecular genotyping assays that detect HPV 16 and 18 would be clinically useful for determining which women should be referred for immediate colposcopy, and which could be followed-up with repeat cytology and high-risk HPV testing in 12 months. Because a U.S. Food and Drug Administration (FDA)-approved HPV genotyping assay was not available in 2006, this recommendation was made contingent on approval of a HPV genotyping assay by the FDA. The first HPV genotyping assay was approved in March 2009 and based on this approval the ASCCP released a Clinical Update on HPV Genotyping and a Management Algorithm for Using HPV Genotyping to Manage HPV High-risk Positive / Cytology Negative Women 30 Years and Older (see the "Availability of Companion Documents" field). This updated information can be found under the heading "2009 Addendum" at the end of the "Major Recommendations" field.

Recommended Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US)

General Management Approaches

A program of DNA testing for high-risk (oncogenic) types of HPV, repeat cervical cytologic testing, or colposcopy are all acceptable methods for managing women over the age of 20 years with ASC-US. **(AI)** When liquid-based cytology is used or when cocollection for HPV DNA testing can be done, "reflex" HPV DNA testing is the preferred approach. **(AI)**

Women with ASC-US who are HPV DNA negative can be followed up with repeat cytologic testing at 12 months. **(BII)** Women who are HPV DNA positive should be managed in the same fashion as women with LSIL and be referred for colposcopic evaluation. **(AII)** Endocervical sampling is preferred for women in whom no lesions are identified **(BII)** and those with an unsatisfactory colposcopy **(AII)** but is acceptable for women with a satisfactory colposcopy and a lesion identified in the transformation zone. **(CII)** Acceptable postcolposcopy management options of women with ASC-US who are HPV positive, but in whom cervical intraepithelial neoplasia (CIN) is not identified, are HPV DNA testing at 12 months or repeat cytological testing at 6 and 12 months. **(BII)** It is recommended that HPV DNA testing not be performed at intervals less than 12 months. **(EIII)**

When a program of repeat cytologic testing is used for managing women with ASC-US, it is recommended that cytologic testing be performed at 6-month intervals until 2 consecutive "negative for intraepithelial lesion or malignancy" results are obtained. **(AII)** Colposcopy is recommended for women with ASC-US or greater cytologic abnormality on a repeat test. **(AII)** After 2 repeat "negative for intraepithelial lesion or malignancy" results are obtained, women can return to routine cytologic screening. **(AII)**

When colposcopy is used to manage women with ASC-US, repeat cytologic testing at 12 months is recommended for women in whom CIN is not identified **(BIII)** Women found to have CIN should be managed according to the 2006 Consensus Guidelines for the Management of Cervical Intraepithelial Neoplasia.

Because of the potential for overtreatment, the routine use of diagnostic excisional procedures such as the loop electrosurgical excision procedure is unacceptable for women with an initial ASC-US in the absence of histologically diagnosed CIN 2,3. **(EII)**

ASC-US in Special Populations

Adolescent Women

In adolescents with ASC-US, follow-up with annual cytologic testing is recommended. **(BII)** At the 12-month follow-up, only adolescents with HSIL or greater on the repeat cytology should be referred to colposcopy. At the 24-month follow-up, those with an ASC-US or greater result should be referred to colposcopy. **(AII)** HPV DNA testing and colposcopy are unacceptable for adolescents with ASC-US. **(EII)** If HPV testing is inadvertently performed, the results should not influence management.

Immunosuppressed and Postmenopausal Women

Human immunodeficiency virus (HIV)-infected, other immunosuppressed women, and postmenopausal women with ASC-US should be managed in the same manner as women in the general population. **(BII)**

Pregnant Women

Management options for pregnant women over the age of 20 years with ASC-US are identical to those described for nonpregnant women, with the exception that it is acceptable to defer colposcopy until at least 6 weeks postpartum. **(CIII)** Endocervical curettage is unacceptable in pregnant women. **(EIII)**

Recommended Management of Women with Atypical Squamous Cells, Cannot Exclude High-Grade Squamous Intraepithelial Lesions (ASC-H)

The recommended management of women with ASC-H is referral for colposcopic evaluation. **(AII)** In women in whom CIN 2,3 is not identified, follow-up with HPV DNA testing at 12 months or cytological testing at 6 and 12 months is acceptable. **(CIII)** Referral to colposcopy is recommended for women who subsequently test positive for HPV DNA or who are found to have ASC-US or greater on their repeat cytologic tests. **(BII)** If the HPV DNA test is negative or if 2 consecutive repeat cytologic tests are negative for intraepithelial lesion or malignancy, return to routine cytologic screening is recommended. **(AI)**

Recommended Management of Women with Low-Grade Squamous Intraepithelial Lesions (LSIL)

Colposcopy is recommended for managing women with LSIL, except in special populations (see following text). **(AII)** Endocervical sampling is preferred for nonpregnant women in whom no lesions are identified **(BII)** and those with an unsatisfactory colposcopy **(AII)**, but is acceptable for those with a satisfactory colposcopy and a lesion identified in the transformation zone. **(CII)** Acceptable postcolposcopy management options for women with LSIL cytology in whom CIN 2,3 is not identified are testing for high-risk (oncogenic) types of HPV at 12 months or repeat cervical cytologic testing at 6 and 12 months. **(BII)** If the HPV DNA test is negative or if 2 consecutive repeat cytologic tests are negative for intraepithelial lesion or malignancy, return to routine cytologic screening is recommended. **(AI)** If either the HPV DNA test is positive or if repeat cytology is reported as ASC-US or greater, colposcopy is recommended. **(AI)** Women found to have CIN should be managed according to the appropriate 2006 Consensus Guidelines on the Management of Cervical Intraepithelial Neoplasia. In the absence of CIN identified histologically, diagnostic excisional or ablative procedures are unacceptable for the initial management of patients with LSIL. **(EII)**

LSIL in Special Populations

Adolescents

In adolescents with LSIL, follow-up with annual cytologic testing is recommended. **(AII)** At the 12-month follow-up, only adolescents with high-grade squamous intraepithelial lesions (HSIL) or greater on the repeat cytology should be referred to colposcopy. At the 24-month follow-up, those with an ASC-US or greater result should be referred to colposcopy. **(AII)** HPV DNA testing is unacceptable for adolescents with LSIL. **(EII)** If HPV DNA testing is inadvertently performed, the results should not influence management.

Postmenopausal Women

Acceptable options for the management of postmenopausal women with LSIL include "reflex" HPV DNA testing, repeat cytological testing at 6 and 12 months, and colposcopy. **(CIII)** If the HPV DNA test is negative or CIN is not identified at colposcopy, repeat cytology in 12 months is recommended. If either the HPV DNA test is positive or the repeat cytology is ASC-US or greater, colposcopy is recommended. **(AII)** If 2 consecutive repeat cytologic tests are negative for intraepithelial lesion or malignancy, return to routine cytologic screening is recommended.

Pregnant Women

Colposcopy is preferred for pregnant, nonadolescent women with LSIL cytology. **(BII)** Endocervical curettage is unacceptable in pregnant women. **(EIII)** Deferring the initial colposcopy until at least 6 weeks postpartum is acceptable. **(BIII)** In pregnant women who have no cytologic, histologic, or colposcopically suspected CIN 2,3 or cancer at the initial colposcopy, postpartum follow-up is recommended. **(BIII)** Additional colposcopic and cytologic examinations during pregnancy are unacceptable for these women. **(DIII)**

Recommended Management of Women with High-Grade Squamous Intraepithelial Lesions (HSIL)

An immediate loop electrosurgical excision or colposcopy with endocervical assessment is an acceptable method for managing women with HSIL, except in special populations (see following text). **(BII)** When CIN 2,3 is not identified histologically, either a diagnostic excisional procedure or observation with colposcopy and cytology at 6 month intervals for 1 year is acceptable, provided in the latter case that the colposcopic examination is satisfactory and endocervical sampling is negative. **(BIII)** In this circumstance it is also acceptable to review the cytological, histological, and colposcopic findings; if the review yields a revised interpretation, management should follow guidelines for the revised interpretation. **(BII)** If observation with cytology and colposcopy is elected, a diagnostic excisional procedure is recommended for women with repeat HSIL cytological results at either the 6 or 12 month visit. **(CIII)** After 1 year of observation, women with 2 consecutive "negative for intraepithelial lesion or malignancy" results can return to routine cytological screening.

A diagnostic excisional procedure is recommended for women with HSIL in whom the colposcopic examination is unsatisfactory, except in special populations (e.g., pregnant women). **(BII)** Women with CIN 2,3 should be managed according to the appropriate 2006 Consensus Guideline for the Management of Women with Cervical Intraepithelial Neoplasia. Ablation is unacceptable in the following circumstances: when colposcopy has not been performed, CIN 2,3 is not identified histologically, or the endocervical assessment identifies CIN of any grade. **(EII)** Triage utilizing either a program of only repeat cytology or HPV DNA testing is unacceptable. **(EII)**

HSIL in Special Populations

Adolescent Women

In adolescents with HSIL, colposcopy is recommended. Immediate loop electrosurgical excision (i.e., "see-and-treat") is unacceptable in adolescent women. **(AII)** When CIN 2,3 is not identified histologically, observation for up to 24 months using both colposcopy and cytology at 6-month intervals is preferred, provided the colposcopic examination is satisfactory and endocervical sampling is negative. **(BIII)** In exceptional circumstances, a diagnostic excisional procedure is acceptable. **(BIII)** If during follow-up a high-grade colposcopic lesion is identified or HSIL cytology persists for 1 year, biopsy is recommended. **(BIII)** If CIN 2,3 is identified histologically, management should follow the 2006 Consensus Guideline for the Management of Women with Cervical Intraepithelial Neoplasia. **(BIII)** If HSIL persists for 24 months without identification of CIN 2,3, a diagnostic excisional procedure is recommended. **(BIII)** After 2 consecutive "negative for intraepithelial lesion or malignancy" results, adolescents and young women without a high-grade colposcopic abnormality can return to routine cytological screening. **(BIII)** A diagnostic excisional procedure is recommended for adolescents and young women with HSIL when colposcopy is unsatisfactory or CIN of any grade is identified on endocervical assessment **(BII)**.

Pregnant Women

Colposcopy is recommended for pregnant women with HSIL. **(AII)** It is preferred that the colposcopic evaluation of pregnant women with HSIL be conducted by clinicians who are experienced in the evaluation of colposcopic changes induced by pregnancy. **(BIII)** Biopsy of lesions suspicious for CIN 2,3 or cancer is preferred; biopsy of other lesions is acceptable **(BIII)**. Endocervical curettage is unacceptable in pregnant women. **(EIII)** Diagnostic excision is unacceptable unless invasive cancer is suspected based on the referral cytology, colposcopic appearance, or cervical biopsy. **(EII)** Reevaluation with cytology and colposcopy is recommended no sooner than 6 weeks postpartum for pregnant women with HSIL in whom CIN 2,3 is not diagnosed. **(CIII)**

Recommended Management of Women with Atypical Glandular Cells (AGC)

Initial Workup

Colposcopy with endocervical sampling is recommended for women with all subcategories of AGC and adenocarcinoma in situ (AIS). **(AII)** Endometrial sampling is recommended in conjunction with colposcopy and endocervical sampling in women 35 years and older with all subcategories of AGCs and AIS. **(BII)** Endometrial sampling is also recommended for women under the age of 35 years with clinical indications suggesting they may be at risk for neoplastic endometrial lesions. These include unexplained vaginal bleeding or conditions suggesting chronic anovulation. It is recommended that women with atypical endometrial cells be initially evaluated with endometrial and endocervical sampling. Colposcopy can be either performed at the initial evaluation or deferred until the results are known. If no endometrial pathology is identified, colposcopy is recommended. **(AII)** If not already obtained, HPV DNA testing at the time of colposcopy is preferred in women with atypical endocervical, endometrial, or glandular cells not otherwise specified (NOS). **(CIII)** The use of HPV DNA testing alone or a program of repeat cervical cytology is unacceptable for the initial triage of all subcategories of AGC and AIS. **(EII)**

Subsequent Evaluation or Follow-up

The recommended postcolposcopy management of women of known HPV status with atypical endocervical, endometrial, or glandular cells NOS who do not have CIN or glandular neoplasia identified histologically is to repeat cytologic testing combined with HPV DNA testing at 6 months if they are HPV DNA positive and at 12 months if they are HPV DNA negative. **(CII)** Referral to colposcopy is recommended for women who subsequently test positive for high risk (oncogenic) HPV DNA or who are found to have ASC-US or greater on their repeat cytologic tests. If both tests are negative, women can return to routine cytologic testing. **(BII)** The recommended postcolposcopy management of women of unknown HPV status with atypical endocervical, endometrial, or glandular cells NOS who do not have CIN or glandular neoplasia identified histologically is to repeat cytologic testing at 6-month intervals. After 4 consecutive "negative for intraepithelial lesion or malignancy" results are obtained, women can return to routine cytologic testing. **(CIII)**

If CIN, but no glandular neoplasia, is identified histologically during the initial workup of a woman with atypical endocervical, endometrial, or glandular cells

NOS, management should be according to the 2006 Consensus Guidelines for the Management of Women with Cervical Intraepithelial Neoplasia. If invasive disease is not identified during the initial colposcopic workup, it is recommended that women with atypical endocervical or glandular cells "favor neoplasia" or endocervical AIS undergo a diagnostic excisional procedure. **(AII)** It is recommended that the type of diagnostic excisional procedure used in this setting provide an intact specimen with interpretable margins. **(BII)** Concomitant endocervical sampling is preferred. **(BII)**

AGC in Special Populations

Pregnant Women

In pregnant women, the initial evaluation of AGC should be identical to that of nonpregnant women, except that endocervical curettage and endometrial biopsy are unacceptable. **(BII)**

Other Forms of Glandular Abnormalities

Benign-Appearing Endometrial Cells

For asymptomatic premenopausal women with benign endometrial cells, endometrial stromal cells, or histiocytes, no further evaluation is recommended. **(BII)** For postmenopausal women with benign endometrial cells, endometrial assessment is recommended regardless of symptoms. **(BII)**

Benign-Appearing Glandular Cells after Hysterectomy

For posthysterectomy patients with a cytologic report of benign glandular cells, no further evaluation is recommended. **(BII)**

Recommended Management of Different Combinations of Results when HPV DNA Testing Is Used as an Adjunct to Cytology in Women 30 Years and Older

General Recommendations

It is recommended that HPV DNA testing target only high-risk (oncogenic) HPV types. There is no clinical utility in testing for other (nononcogenic) types. **(AI)** Testing for other (nononcogenic) HPV types when screening for cervical neoplasia, or during the management and follow-up of women with abnormal cervical cytology or cervical neoplasia, is unacceptable. **(EI)**

Recommendations for Women with Different Combinations of Results

For women 30 years of age and older who have a cytology result of "negative for an intraepithelial lesion or malignancy" but test positive for HPV, repeat cytology and HPV testing at 12 months is preferred. **(BII)** If on repeat testing HPV is detected, colposcopy is recommended. **(AII)** Women found to have an abnormal result on repeat cytology should be managed according to the appropriate 2006 Consensus Guidelines outlined earlier.

Recommendations for HPV Genotyping*

Until a Food and Drug Administration (FDA)-approved assay becomes available, a recommendation for use of type-specific HPV genotyping cannot be made. Once such assays are FDA approved, emerging data support the triage of women 30 years of age and older with a cytology result of "negative for an intraepithelial lesion or malignancy" but who are HPV positive with HPV genotyping assays to identify those with HPV 16 and 18. **(AII)**

***2009 Addendum**

Descriptions of New FDA-approved HPV DNA Tests

In March 2009 the FDA announced approval for clinical use in the U.S. of two new HPV DNA diagnostic tests. One of these tests is designed to identify 14 high risk types of HPV. These include the 13 types detected by the Hybrid Capture® 2 HPV DNA Assay (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) as well as HPV 66. This test will be marketed under the name Cervista™ HPV HR. The other test is designed to specifically detect HPV 16 and HPV 18 and will be marketed under the name Cervista™ HPV 16/18. Both tests utilize an isothermal enzymatic DNA amplification process with a fluorescent read out and both are approved for use with ThinPrep® samples. They were developed by Third Wave Technologies which was acquired in 2008 by Hologic Inc., the manufacturer of the ThinPrep® Pap test.

FDA Approved Indications

The FDA-approved clinical indications for Cervista™ HPV HR are similar to those of the Hybrid Capture® 2 HPV DNA Assay. These are:

1. To screen patients with ASC-US cervical cytology results to determine the need for referral to colposcopy
2. Used adjunctively with cervical cytology to screen women 30 years and older to assess the presence or absence of high-risk HPV types

The FDA-approved indications for the Cervista™ HPV 16/18 test are:

1. In women 30 years and older the test may be used adjunctively with the Cervista™ HPV HR test in combination with cervical cytology to assess the presence or absence of specific high-risk HPV types.
2. Used adjunctively with the Cervista™ HPV HR test in patients with ASC-US cervical cytology results, to assess the presence or absence of specific high-risk HPV types. The results of this test are not intended to prevent women from proceeding to colposcopy.

ASCCP 2006 Consensus Conference Recommendations for HPV 16/18 Detection

The clinical utility of HPV genotyping assays was discussed at the 2006 ASCCP Consensus Conference. At the time of the conference it was recognized that molecular genotyping tests would become commercially available for routine

clinical use in the near future. Therefore the data available at that time was evaluated and recommendations made that were contingent on a FDA-approved genotyping assay becoming available.

Use When Screening Women 30 Years and Older

Based on the data available in 2006, it was determined that in cytology negative women 30 years and older who are HPV DNA positive (for any of the 13 or 14 high-risk types of HPV detected by the high-risk HPV assays) molecular genotyping assays that detect HPV 16 and 18 would be clinically useful for determining which women should be referred for immediate colposcopy, and which could be followed-up with repeat cytology and high-risk HPV testing in 12 months. See Figure 1 in the 2009 Addendum.

Use for Women with ASC-US

Based on the data available as of September 2006, both the committee that reviewed atypical squamous cells and the committee that reviewed HPV DNA testing decided that HPV genotyping does not add clinical benefit to the management of women with ASC-US. This was based on the fact that only approximately 50% of CIN 2+ lesions are associated with infection with HPV 16 or 18. The other 50% are not. In ALTS, for women 21 years of age and older with oncogenic HPV-positive ASCUS, the overall two-year cumulative risk of CIN 2+ was 25%. Stratifying by HPV genotype categories, the cumulative risk of CIN 2+ for women with HPV 16/18-positive ASCUS was approximately 40%, while the risk for women with other oncogenic (non 16/18) HPV-positive ASCUS was approximately 20%. Similar patterns were observed in women aged 21-29 and women aged 30 and older. While HPV genotyping did stratify risk to an extent, the risk of CIN 2+ among women with non 16/18 oncogenic HPV-positive ASCUS remained high enough to warrant colposcopy. **Therefore the 2006 ASCCP guidelines do NOT recommend the use of HPV genotyping in women with oncogenic HPV-positive ASC-US.** Management of women in the general population with ASC-US, who are screened using liquid-based cytology should be to perform a "reflex" test using a validated assay that detects either 13 or 14 high-risk HPV types. If the woman is high-risk HPV DNA positive, she should be referred to colposcopy, even if she tests negative for HPV 16 and HPV 18.

Data from the pivotal trial of the new HPV genotyping assay for HPV 16/18 that led to the FDA-approved indication of using 16/18 genotyping in women with ASCUS has not yet been published. Once available, this data, as well as data from the ongoing clinical trials of genotyping tests being developed by other companies, may necessitate changes in the management guidelines.

Situations Where HPV DNA Testing and Genotyping Are Not Recommended

As HPV DNA testing becomes more widespread we need to remember that there are situations where high-risk HPV DNA testing and genotyping are NOT recommended. These include:

- Adolescents, defined as women 20 years and younger (regardless of their cytology results)

- Women 21 years and older with ASC-H, LSIL, or HSIL cytology (note: "reflex" HPV testing is acceptable in postmenopausal women with LSIL)
- Routine screening in women before the age of 30 years
- In women considering vaccination against HPV
- For routine STD screening
- As part of a sexual assault workup
- HPV genotyping is not recommended for women with ASC-US
- HPV genotyping is not recommended as the initial screening test for women 30 years and older

It should also be recognized that there are situations where the 2006 Consensus Guidelines recommend limits on the frequency of HPV DNA testing to avoid over-testing and unnecessary treatment. When managing women with ASC-US it is recommended that HPV DNA testing not be performed at intervals of less than 12 months. In addition, women 30 years of age and older who are negative by both cytology and high-risk HPV DNA testing should not be rescreened (using either cervical cytology or HPV DNA testing) before 3 years.

Definitions:

Strength of Recommendation*

- A. Good evidence for efficacy and substantial clinical benefit support recommendations for use.
- B. Moderate evidence for efficacy or only limited clinical benefit supports recommendation for use.
- C. Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds.
- D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.
- E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

Quality of Evidence*

- I. Evidence from at least one randomized controlled trial.
- II. Evidence from at least one clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), or from multiple time-series studies, or dramatic results from uncontrolled experiments.
- III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

Terminology**

Recommended: Good data to support use when only one option is available.

Preferred: Option is the best (or one of the best) when there are multiple other options.

Acceptable: One of multiple options when there are either data indicating that another approach is superior or when there are no data to favor any single option.

Unacceptable: Good data against use.

*Modified from Gross PA, Barrett TL, Dellinger EP, et al. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Dis 1994;18:421 and Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001;32:8511.

**The assignment of these terms represents an opinion ratified by vote by the Consensus Conference.

CLINICAL ALGORITHM(S)

Algorithms for the following are available from the [American Society for Colposcopy and Cervical Pathology Web site](#):

- Management of women with atypical squamous cells of undetermined significance (ASC-US)
- Management of adolescent women with either atypical squamous cells of undetermined significance (ASC-US) or low-grade squamous intraepithelial lesion (LSIL)
- Management of women with atypical squamous cells: cannot exclude high-grade SIL (ASC-H)
- Management of women with low-grade squamous intraepithelial lesion (LSIL)
- Management of pregnant women with low-grade squamous intraepithelial lesion (LSIL)
- Management of women with high-grade squamous intraepithelial lesion (HSIL)
- Management of adolescent women (20 years or younger) with high-grade squamous intraepithelial lesion (HSIL)
- Initial workup of women with atypical glandular cells (AGC)
- Subsequent management of women with atypical glandular cells (AGC)
- Use of HPV DNA testing as an adjunct to cytology for cervical cancer screening in women 30 years and older

2009 Addendum

An algorithm on the use of HPV genotyping to manage HPV HR positive/cytology negative women 30 years and older is available from the [American Society for Colposcopy and Cervical Pathology Web site](#).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Although the guidelines are based on evidence whenever possible, for certain clinical situations, there is limited high quality evidence, and in these situations the guidelines have, by necessity, been based on consensus expert opinion.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of women with abnormal cervical cancer screening tests

POTENTIAL HARMS

Not stated

CONTRAINDICATIONS

CONTRAINDICATIONS

Endocervical curettage is contraindicated in pregnant patients.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- It is important to recognize that these guidelines should never substitute for clinical judgment. Clinical judgment should always be used when applying a guideline to an individual patient because it is impossible to develop guidelines that apply to all situations.
- The current guidelines expand clinical indications for human papillomavirus (HPV) testing based on studies using validated HPV assays. One cannot assume that management decisions that are based on results of HPV tests that have not been similarly validated will result in the outcomes that are intended by these guidelines. Furthermore, the application of these guidelines using such tests may increase the potential for patient harm. The appropriate use of these guidelines requires that laboratories utilize only HPV tests that have been analytically and clinically validated with proven acceptable reproducibility, clinical sensitivity, specificity, and positive and negative predictive values for cervical cancer and verified precancer (CIN 2,3), as documented by Food and Drug Administration (FDA) approval and/or publication in peer-reviewed scientific literature. It is also important to stress that testing should be restricted to high-risk (oncogenic) HPV types. Testing for low-risk (nononcogenic) HPV types has no role in the evaluation of women with abnormal cervical cytological results. Therefore, whenever "HPV testing" is referred to in the guidelines, it applies only to testing for high-risk (oncogenic) HPV types.

2009 Addendum

This Clinical Update has been designed as an educational resource and as such does not define a standard of care, nor is it intended to dictate an exclusive course of treatment or procedure to be followed. It presents methods and techniques of clinical practice that are acceptable and used by recognized authorities, for consideration by licensed healthcare professionals to incorporate into their practice. Variations of practice, taking in account the needs of the

individual patient, resources, and limitations unique to the institution or type of practice, may be appropriate.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards
Resources
Wall Poster

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. 2009 addendum. Hagerstown (MD): American Society for Colposcopy and Cervical Pathology; 2009. 3 p. [5 references]

Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D, 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. Am J Obstet Gynecol 2007 Oct;197(4):346-55. [81 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Apr 24 (revised 2007 Oct; addendum released 2009)

GUIDELINE DEVELOPER(S)

American Society for Colposcopy and Cervical Pathology - Medical Specialty Society

GUIDELINE DEVELOPER COMMENT

Participating organizations include: American Academy of Family Physicians; American Cancer Society; American College Health Association; American College of Obstetricians and Gynecologists; American Social Health Association; American Society for Clinical Pathology; American Society for Colposcopy and Cervical Pathology; American Society of Cytopathology; Association of Reproductive Health Professionals; Centers for Disease Control and Prevention, Division of Viral and Rickettsial Disease; Centers for Disease Control and Prevention, Division of Cancer Prevention and Control; Centers for Disease Control and Prevention, Division of Laboratory Systems; Centers for Medicaid and Medicare Services; College of American Pathologists; Food and Drug Administration; International Academy of Cytology; International Federation for Cervical Pathology and Colposcopy; International Federation of Gynecology and Obstetrics; International Gynecologic Cancer Society; International Society of Gynecological Pathologists; National Cancer Institute; National Association of Nurse Practitioners in Women's Health; Papanicolaou Society of Cytopathology; Pan American Health Organization; Planned Parenthood Federation of America; Society of Canadian Colposcopists; Society of Gynecologic Oncologists; Society of Gynecologic Oncologists of Canada; Society of Obstetricians and Gynaecologists of Canada

SOURCE(S) OF FUNDING

American Society for Colposcopy and Cervical Pathology

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: Thomas C. Wright Jr, MD, Department of Pathology, College of Physicians and Surgeons of Columbia University, New York, NY; L. Stewart Massad, MD, Department of Obstetrics and Gynecology, Washington University School of Medicine, St Louis, MO; Charles J. Dunton, MD, Department of Obstetrics and Gynecology, Lankenau Hospital, Wynnewood, PA; Mark Spitzer, MD, Department of Obstetrics and Gynecology, Brookdale University Hospital and Medical Center, Brooklyn, NY; Edward J. Wilkinson, MD, Department of Pathology, University of Florida College of Medicine, Gainesville, FL; Diane Solomon, MD, National Institutes of Health and National Cancer Institute, Bethesda, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wright TC Jr, Cox JT, Massad LS, Twiggs LB, Wilkinson EJ. 2001 Consensus Guidelines for the management of women with cervical cytological abnormalities. JAMA 2002 Apr 24;287(16):2120-9.

GUIDELINE AVAILABILITY

Electronic copies of the original guideline and the 2009 addendum: Available from the [American Society for Colposcopy and Cervical Pathology \(ASCCP\) Web site](#).

Print copies: Available from the American Society for Colposcopy and Cervical Pathology, 20 West Washington St., Suite 1, Hagerstown, MD 21740.

AVAILABILITY OF COMPANION DOCUMENTS

The 2006 consensus guideline speaker's kit, pocket-sized versions of the algorithms, and algorithm wall charts are available for purchase from the [American Society for Colposcopy and Cervical Pathology \(ASCCP\) Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 13, 2002. This summary was updated by ECRI on September 13, 2002. It was verified by the guideline developer on November 19, 2002. This NGC summary was updated by ECRI Institute on April 8, 2009. This NGC summary was updated by ECRI Institute on June 30, 2009. The updated information was verified by the guideline developer on July 8, 2009.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public

or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

[Copyright/Permission Requests](#)

Date Modified: 8/3/2009

